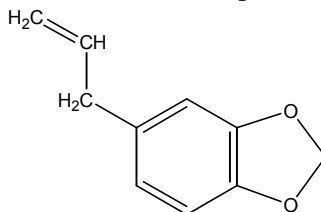


**SAFROLE**  
**CAS No. 94-59-7**

First Listed in the *Second Annual Report on Carcinogens*



## CARCINOGENICITY

Safrole is *reasonably anticipated to be a human carcinogen* based on sufficient evidence for the carcinogenicity of in experimental animals (IARC V.10, 1976). When given by gavage followed by dietary administration, safrole increased the incidences of liver cell tumors in mice of both sexes. When administered in the diet, safrole increased the incidences of liver hepatocellular carcinomas and cholangiocarcinomas in rats of both sexes and hepatocellular carcinomas in male mice. When administered to infant mice by subcutaneous injection, safrole induced lung adenomas and adenocarcinomas in mice of both sexes and hepatomas in male mice.

There are no data available to evaluate the carcinogenicity of safrole in humans (IARC V.10, 1976).

## PROPERTIES

Safrole is a clear, colorless to slightly yellow liquid with an odor of sassafras. It is insoluble in water and very soluble in alcohol. Safrole is combustible when exposed to heat or flame, and when heated to decomposition it emits acrid smoke and fumes.

## USE

Safrole, a naturally occurring substance, has been used as a flavoring agent in drugs, beverages, and foods and in the manufacture of heliotropin (IARC V.10, 1976). In 1983, the FDA reported that safrole or sassafras, the extract or the oil, was reported to be an ingredient in 113 over-the-counter drug formulations, generally for topical application but occasionally for oral administration. Safrole reportedly is also used in soap and perfumes and as a flavoring agent in drugs (IARC V.10, 1976). Formerly, it was an ingredient in pesticides.

## PRODUCTION

The USITC does not identify any companies currently producing safrole in the United States. Approximately 36,000 lb of safrole were imported from Brazil in 1980. The 1979 TSCA Inventory identified four companies producing 2.8 million lb of dihydrosafrole, with some site limitations in 1977. It also identified three companies producing 55,000 lb of isosafrole and four companies importing 1,000 lb. The CBI Aggregate for isosafrole was less than one million lb (TSCA, 1979).

## EXPOSURE

The primary routes of potential human exposure to safrole are ingestion of foods, drugs, and beverages containing it and dermal contact. In atmosphere it will exist in vapor phase and in water it will adsorb. FDA indicated that exposure of the general population to safrole through food consumption was extremely low because FDA prohibited its use in food. Minimal exposure may occur through the use of edible spices, including nutmeg and mace, which contain low levels of naturally occurring safrole (IARC V.1, 1972). The compound does not pose a hazard to the general population through consumption of drinking water because of its insolubility in water. Potential occupational exposure to workers handling safrole may occur through dermal contact. Health professionals (e.g., pharmacists, physicians, and nurses) may possibly be exposed during formulation, preparation, administration, or clean-up of drugs containing safrole or sassafras. In 1981, OSHA estimated that 30 workers were possibly exposed to safrole. The Toxic Chemical Release Inventory (EPA) listed two industrial facilities that produced, processed, or otherwise used safrole in 1996 (TRI, 1990). In compliance with the Community Right-to-Know Program, these facilities reported releases to the environment which were estimated to total 505 lb.

## REGULATIONS

EPA has promulgated standards for voluntary cancellation of safrole in pesticide products under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). EPA permitted one registrant to distribute and sell one safrole-containing product until 3/11/78, but after that no stocks were available for pesticide use. EPA regulates safrole under the Resource Conservation and Recovery Act (RCRA) and the Superfund Amendments and Reauthorization Act (SARA). RCRA designates safrole as a hazardous constituent of waste and it is subject to reporting rules under RCRA and SARA. A final rule reportable quantity (RQ) of 100 lb has been established under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). FDA banned the use of oil of safrole and sassafras bark in food, but permits use of edible spices, such as nutmeg and mace, which contain very small quantities of naturally occurring safrole. FDA is reviewing the use of safrole in sleeping aids and sedatives. OSHA regulates safrole under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-132.